In the Specification:

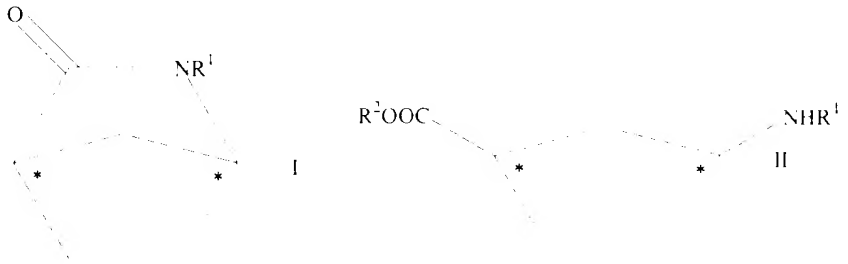
Please insert the following paragraph on page 1, after the title:

--CROSS-REFERENCE TO RELATED APPLICATIONS

This application is a national phase application of International Application No. PCT/EP99/04814, which was filed on July 8, 1999 and which published on January 20, 2000, which in turn claims priority from European Application No. 98112719.4, which was filed on July 9, 1998, and European Application No. 98123949.4, which was filed on December 17, 1998.--

Please replace the paragraph beginning on page 1, last line, above formulas I and II, with the following rewritten paragraph:

--The invention's method for preparing compounds of the general formulas



I II

and

wherein R^1 is acyl , alkoxycarbonyl or aryloxycarbonyl and R^2 is a hydrogen atom or C_{1-10} alkyl, comprises treating with a hydrolase and an effective amount of a nucleophile and a base in a constant pH range a racemic lactam of the formula

III

Please replace the sixth full paragraph on page 2 with the following rewritten paragraph:

--Hydrolases that can be used are proteases or lipases, preferably proteases, such as serine proteases. Examples of serine proteases that can be used are chymotrypsins, trypsins and subtilisins (bacterial serine proteases). Subtilisins that can be used are commercial subtilisins, such as subtilisin A, subtilisin B, alcalases, ALK enzymes, bacillopeptidase A, bacillopeptidase B, bioprases, colistinases, esperases, genenase I, kazusase, maxacal, maxatases, nagarses, peptidases, protease S, protease VIII, protease XXVII, proteinases, such as the alkaline proteinase of Bacillus subtilis or Aspergillus oryzae, proteinase K from Tritirachium album, savinases, subtilopeptidasen, superases, and thermoases. Conducting the biotransformation by means of savinases is preferred. Suitable savinases are savinase 12 Type W™, savinase 16.OL Type EX™, savinase 32.OL Type EX™, savinase 4.OT Type W™, and savinase 8.OL™. The lipase that can be used is, for example, lipase from Candida Antarctica.--

Please replace the paragraph beginning on page 2, four lines from the bottom, with the following rewritten paragraph:

--If the hydrolases used are proteases, such as proteases from Bacillus subtilis, proteases from Aspergillus oryzae, proteinase K from Tritirachium album, the (1S, 4R) enantiomer in the racemic lactam of formula III is hydrolyzed suitably into the corresponding compound of general formula II, whereby the (1R, 4S) enantiomer of general formula I is obtained. If the hydrolases used are lipases, such as lipase from Candida Antarctica, the (1R, 4S) enantiomer in the racemic lactam of formula III is hydrolyzed suitably into the corresponding compound of general formula II, whereby the (1S, 4R) enantiomer of general formula I is obtained.--

Please replace the first full paragraph on page 3 with the following rewritten paragraph:

--Water or C_{1-10} alcohols can be used as the nucleophile. Suitable C_{1-10} alcohols are methanol, ethanol, propanol, isopropanol, butanol, *t*-butanol, isobutanol, pentanol, hexanol,

heptanol, octanol, nonanol or decanol. If the nucleophile used is a C_{1-10} alcohol, the corresponding ester of general formula II (R^2 = C_{1-10} alkyl) is formed, as the expert knows. If water is used as the nucleophile, obviously, the corresponding acid of general formula II (R^2 = H) is formed.--

Please replace the fifth full paragraph on page 3 with the following rewritten paragraph:

--The biotransformation is suitably conducted in water, a buffer solution, a C_{1-10} alcohol or in a mixture of these with an aprotic organic solvent. Suitable aprotic organic solvents are, for example, ether and aromatic hydrocarbons. Tetrahydrofuran, dioxane or t-butyl methyl ether can be used as the ether. Toluene and benzene are suitable aromatic hydrocarbons. The buffer solutions used can be, for example, low molarity, such as 10-100 mM sodium or potassium phosphate buffer, hepes buffer. The C_{1-10} alcohols used can be those previously described.--

Please replace the paragraph beginning on page 3, two lines from the bottom, with the following rewritten paragraph:

--After a usual conversion time of a few hours depending on the selected starting material, the desired optically active compounds of general formulas I and II are obtained in outstanding yields and enantiomer purity. The preferred starting materials are racemic 2-acetyl-2-azabicyclo-[2.2.1]hept-5-ene-3-one (R^1 = acetyl) and the racemic 2-ethoxycarbonyl-2-azabicyclo-[2.2.1]hept-5-ene-3-one (R^1 = ethoxycarbonyl). The preferred compounds of formula II are (1S, 4R)-4-acetylamino-2-cyclopentene-1-carboxylic acid (R^1 = acetyl, R^2 = H), (1S, 4R)-4-ethoxycarbonylamino-2-cyclopentene-1-carboxylic acid (R^1 = ethoxycarbonyl, R^2 = H), (1S, 4R)-4-acetylamino-2-cyclopentene-1-carboxylic acid methyl ester (R^1 = acetyl, R^2 = CH_3), (1S, 4R)-4-acetylamino-2-cyclopentene-1-carboxylic acid butyl ester (R^1 = acetyl, R^2 = C_4H_9), (1S, 4R)-4-acetylamino-2-cyclopentene-1-carboxylic acid ethyl ester (R^1 = acetyl, R^2 = C_2H_5), and (1S, 4R)-4-acetylamino-2-cyclopentene-1-carboxylic acid propyl ester (R^1 = acetyl, R^2 = C_3H_7).

The (1S, 4R)-4-acetylamino-2-cyclopentene-1-carboxylic acid C_{2-10} alkyl esters, preferably the (1S, 4R)-4-acetylamino-2-cyclopentene-1-carboxylic acid ethyl ester and the (1S, 4R)-4-acetylamino-2-cyclopentene-1-carboxylic acid propyl ester of the formula II are not described in the literature and are similarly part of the invention.--

Please replace the third full paragraph on page 4 with the following rewritten paragraph:

--The binary alkali metal borohydrides or alkaline earth metal borohydrides used can be $NaBH_4$, $LiBH_4$, KBH_4, $NaAlH_4$, $LiAlH_4$, $KAlH_4$, $Mg(BH_4)_2$, $Ca(BH_4)_2$, $Mg(AlH_4)_2$, $Ca(AlH_4)_2$. Complex metal hydrides of the boron or aluminum group can have the general formula $M^1M^2H_nL_m$, wherein n is a whole number from 1 to 4, m is a whole number from 4 to 4-n, M^1 is an alkali metal atom, M^2 is boron or aluminum, and L is C_{1-4} alkyl, C_{1-4} alkenyl, C_{1-4} alkoxy, CN or an amine, or the complex metal hydrides can have the general formula $M^2H_OL_p$, wherein M^2 is as already named, o is a whole number from 0 to 3, and p is a whole number from 3 to 3-o. The $M^1M^2H_nL_m$ used can be $LiBH(C_2H_5)_3$, $LiBH_x(OCH_3)_{4-x}$, wherein x is a whole number from 1 to 3, $LiAlH(OC(CH_3)_3)_3$, $NaAlH_2(OC_2H_4OCH_3)_2$, $NaAlH_2(C_2H_5)_2$ or $NaBH_3CN$. The reduction is conducted preferably with a metal borohydride, such as sodium borohydride.--

Please replace the fourth full paragraph on page 10 with the following rewritten paragraph:

--1.3 Reduction of (1R,4S)-2-acetyl-2-azabicyclo[2.2.1]hept-5-ene-3-one to (1R,4S)-1-acetylamino-4-(hydroxymethyl)-2-cyclopentene.--

Please replace the paragraph beginning on page 10, six lines from the bottom with the following rewritten paragraph:

--287.4 g (-)-acetyl-2-azabicyclo[2.2.1]hept-5-ene-3-one (100% ==> -255 ml, 97%; 1.9 moles) were dissolved in 380 ml water and 1217 ml 2-butanol. The solution was cooled to 0 to 2 °C. 45 g $NaBH_4$ (1.188 moles, 1.25 eq.) were suspended in 304 ml fresh 2-butanol in another stirring device. The $NaBH_4$ suspension was added to the solution during 1- 2 hours. The reaction was exothermic, and the temperature was not allowed to exceed 5 °C. The

temperature had to be at 0° C before a portion was added. The reaction was followed by DC (thin-layer chromatography) (hexane/etrol/MeOH: 5 5 1). The reaction was allowed to continue for 1 to 2 hours after the addition. When the reaction was complete (educt concentration had to be at < 1.0 %), the pH was adjusted to 2 with ca. 135 g concentrated hydrochloric acid. The temperature was maintained below 10°C. The pH was then adjusted immediately to 9 with ca. 85 ml 30% sodium hydroxide solution. The precipitated salts were filtered and washed with 127 ml fresh 2-butanol. The filtrate and the "2-butanol wash" were combined, and the phases separated. The aqueous phase was extracted twice with 380 ml fresh 2-butanol each time. The 2-butanol phases were combined. Ca. 2450 g of a 10% solution of the product, (1R,4S)-1-acetylamino-4-(hydroxymethyl)-2-cyclopentene, were obtained in 2-butanol. This corresponded to ca. 250 g of 100% product, (1R,4S)-1-acetylamino-4-(hydroxymethyl)-2-cyclopentene, corresponding to a yield of 85%.--

Please replace the first full paragraph on page 11 with the following rewritten paragraph:

--1.4 Hydrolysis of (1R,4S)-1-acetylamino-4-(hydroxymethyl)-2-cyclopentene to (1R,4S)-1-amino-4-(hydroxymethyl)-2-cyclopentene.--

Please replace the second full paragraph on page 11 with the following rewritten paragraph:

--1.4.1 30% NaOH (45 g) was added to 49.3 g (0.28 mole) (1R, 4S)-1-acetylamino-4-(hydroxymethyl)-2-cyclopentene, and the suspension was heated to 100 °C. After 3.5 hours, the solution was cooled to 0°C and then adjusted to pH = 1.0 with concentrated HCl. Water was evaporated and NaCl filtered off. Pentanol (2 ml per go of residue) and acetone (6 ml per gram of residue) were added. The resulting precipitate was filtered and washed with 20 ml acetone. 37.5 g (0.24 mole) of product were obtained as the hydrochloride salt having an ee = 99%, corresponding to a yield of 86%.--

The third full paragraph on page 11 has been amended as follows:

--1.4.2 85.4 g (1R,4S)-(-)-1-acetylamino-4-(hydroxymethyl)-2-cyclopentene 100% (0.55 mole) was prepared as a 10% solution in 2-butanol. It was distilled until the distillate ceased. Then 100.0 g of a 30% sodium hydroxide solution (==> 33.0 g NaOH 100%; 0.825 mole, 1.5 eq) and 65 g water were added. The remaining 2-butanol was removed (with ca.l 10 g water) by azeotropic distillation. The solution was heated at reflux (100 – 100° C) for 4-5 hours. The reaction was followed by GC. When the conversion was complete, the reaction was cooled to 50° C, and 154 ml 2-butanol (124.3 g) were added. The phases were separated at 50 °C 915 minutes stirring, phases separate). The aqueous phase (ca. 165 g) was discarded. The organic phasese were combined, and ca. 22 g hydrogen chloride were added at 20 – 40 °C to make pH 1. Some salts precipitated during the acidification. These salts were filtered off at 20°C, and the filtrate was distilled under standard pressure until 220 ml distillate (ca. 180 g) were collected (boiling temperature ca. 91- 92 °C). At ca. 70° C, 176 ml acetone (139.0 g) were added. The suspension was stirred at reflux for 15-30 minutes and then cooled to - 5°C. After 1 hour at this temperature was filtered off by suction, and the filter cake was washed with 154 ml acetone. 70 g of (-) of 100 % product were obtained, corresponding to a yield of 85%.--

Please replace the third full paragraph on page 12 with the following rewritten paragraph:

--109.13 g racemic 2-azabicyclo[2.2.1]hept-5-ene-3-one were mixed with 182.1 g triethylamine, 6.11 g 4-dimethylaminopyridine and 500 ml acetonitrile. The reaction was heated to 50° C. Then, 195.3 g ethyl chloroformate, dissolved in 150 ml acetonitrile, were added portionwise. The temperature was maintained below 55° C. After the reaction ended, the solution was cooled to 20° C. The salts were filtered off and washed with acetonitrile. The filtrate was concentrated at 60° C and 20 mbar, and then mixed with 1500 ml toluene. Three extractions followed: with 250 ml water, pH 8, with 250 ml acetic acid (1%) and with 250 ml saturated NaCl solution. The organic phase was dried with $MgSO_4$ and concentrated at 80° C/20 mbar. 167.4 g of a brown oil were obtained. The content by GC was 96% (±)-2-